Organochlorines in Carpet Dust and Non-Hodgkin Lymphoma

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Background: The incidence of non-Hodgkin lymphoma (NHL) has risen over the past several decades. Reasons for this increase are largely unexplained.

Methods: In this population-based case–control study, we examined NHL risk and exposure to organochlorine compounds using concentrations in carpet dust as an exposure indicator. We identified NHL cases, uninfected with HIV, diagnosed between 1998 and 2000 among women and men ages 20–74 years in Iowa, Los Angeles County, and the Detroit and Seattle metropolitan areas. Controls were selected using random-digit-dialing or Medicare files. Organochlorine concentrations were measured in vacuum bag dust from 603 white cases and 443 white controls who had owned most of their carpets for at least 5 years.

Results: NHL risk was elevated if any of the polychlorinated biphenyl (PCB) congeners (PCBs 105, 138, 153, 170, or 180) was detected (odds ratio = 1.5; 95% confidence interval = 1.2–2.0). Risk was elevated in the top tertile of PCB 180 (1.7; 1.1–2.6) and in the top 2 tertiles of total PCBs (middle tertile, 1.6 [1.1–2.4]; top tertile 1.5 [1.0–2.2]). There was a positive trend in risk with increasing PCB 180 levels (P trend = 0.03). NHL risk was elevated if dichlorodiphenyldichloroethylene (DDE) was detected (1.3; 1.0–1.7), but only among men. A positive, but not monotonic, dose–response relationship was observed for DDE (P trend = 0.02).

Conclusions: Our findings suggest an increased risk of NHL associated with exposure to PCBs, with evidence of greater effects for PCB 180. There is also some evidence of an association with DDE.

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The incidence of non-Hodgkin lymphoma (NHL) has risen in many countries over the past several decades.[1,2] Although this increase is partially attributable to changing diagnostic patterns, use of immunosuppressive drugs, and increasing rates of HIV infection, a substantial portion remains unexplained.[3]

Organochlorine compounds such as dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs) are ubiquitous environmental pollutants that accumulate in adipose tissue. Several case–control studies[4–9] have reported an elevated risk of NHL after exposure to DDT or chlordane. Case–control studies with biologic samples[10–12] have found positive associations between blood or adipose levels of PCBs and risk of NHL. Although some studies have reported increased NHL risk after occupational exposure to pentachlorophenol and other chlorophenates,[5,13] these studies are difficult to interpret because commercial grades of these compounds contain contaminants such as polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans.[14]

PCBs were produced in the United States from 1929 until 1977.[15] They were originally used mainly in closed systems such as electrical transformers and capacitors. Use in other products such as hydraulic fluids, plasticizers, flame retardants, paints, wood preservatives, and pesticides became widespread after 1957.[16] PCBs were released into the environment during their manufacture and disposal, and during the production, use, repair, and disposal of PCB-containing products. PCB levels have decreased in most environmental media in the past 2 decades, as have PCB body burdens in humans.[15]

DDT was first used in 1939; its use peaked in the early 1960s and it was banned in the United States in 1972. DDT was used extensively as an agricultural insecticide and vector

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control agent, and was also used to control lice, household and fabric pests, and lawn and garden pests.[17] Concentrations of DDT in all media have declined since this chemical was banned.[18] DDE is slowly formed from the breakdown of DDT in the natural environment in the presence of sunlight, microorganisms, and moisture. DDE itself has never been used commercially.

Production of the insecticide chlordane began in the United States in 1947.[10] Chlordane was widely used by pest control operators, on agricultural crops, on home lawns and gardens, and on turf and ornamentals. Between 1983 and 1988, chlordane use was restricted to subterranean termite control. All commercial uses were discontinued in the United States in 1988.

Pentachlorophenol, first introduced in 1936, has been used as an insecticide, fungicide, herbicide, molluscicide, algicide, disinfectant, and ingredient in antifouling paint. Its use was restricted to certified pesticide applicators in 1984. Currently, its main use is as a wood preservative.[14]

We report here on a population-based case–control study of adult NHL. Carpet dust samples were collected from participants' homes and analyzed for organochlorine pesticides, PCBs, and other substances. Organochlorines may persist for years in carpets, where they are protected from degradation by sunlight, rain, and most microbial action.[19] Because carpets act as long-term repositories for these chemicals, their levels in carpet dust may reflect exposures occurring over the lifetime of the carpet. This article examines the association between organochlorine concentrations in dust and NHL risk.

METHODS

Study Population and Data Collection

This study was conducted in 4 areas covered by the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute: Iowa, Los Angeles County, and the metropolitan areas of Detroit and Seattle. Eligible cases were men and women age 20–74 years newly diagnosed with a first primary NHL between July 1998 and June 2000. In Iowa and Seattle, all consecutive cases were chosen, nearly all of whom were white. In Detroit and Los Angeles, all black cases but only a random sample of white cases was chosen (maximizing the number of blacks). Controls were selected from the general population during the same time period as the cases, frequency-matched on age, sex, race, and center. Controls under age 65 were identified by random-digit-dialing and those age 65 and older were identified from Medicare files. HIV-infected individuals were excluded. Pathology reports were obtained and classified according to the latest World Health Organization scheme (ICD-O-3 codes 967–972). The study was approved by human subjects review boards at all institutions, and written informed consent was obtained from each participant before interview.

Computer-assisted personal interviews were conducted in participants' homes. We asked each interviewed subject for permission to collect a dust sample, and those who consented were screened for eligibility. Subjects were eligible if they had used their vacuum cleaner within the past year and had owned at least half of their carpets or rugs for 5 years or more. Used vacuum bags were removed from the vacuum cleaner, shipped overnight in insulated boxes to Southwest Research Institute (San Antonio, TX), and placed in freezers.

We were unable to recruit and obtain dust samples from enough nonwhites to allow for a meaningful analysis. Therefore, this analysis is limited to white cases and controls. Of 1455 eligible cases, 187 were deceased, could not be located, had moved out of the area, or had physician refusal. We attempted to contact the remaining 1268 (87%) and were successful in interviewing 1123 (89% of those we attempted to contact). Of 1568 eligible controls, we attempted to contact 1401 (89%) and were able to interview 843 (60% of those we attempted to contact). We obtained consent for dust samples from 1058 cases and 814 controls (94% and 97% of those interviewed), and 618 cases and 452 controls (58% and 56% of those who consented) were eligible for dust sampling.

Laboratory Analysis

Portions of dust from each vacuum cleaner bag were passed through a 100-mesh sieve to remove large particles such as human hair. The fine fraction (<150 μm) was split into aliquots and frozen. Samples were grouped into batches of 13–15 samples for extraction and analysis with at least 4 cases and 4 controls in each batch. Laboratory personnel were unaware of case–control status. Extraction and analysis were performed on samples from 603 cases and 443 controls (98% of both); the remainder was lost in shipping or laboratory accidents, arrived at the laboratory with missing labels, or had insufficient dust for analysis.

Two different extractions were performed on separate 2-g aliquots of each dust sample, one for neutral-extractable analytes and one for acid-extractable analytes. Technicians spiked each aliquot with appropriate surrogates before extraction. Details of the spiking and extraction procedures are described by Colt et al.[20] There were 37 neutral-extractable compounds, including 15 organochlorine compounds, 10 of which have been used as pesticides (aldrin, dieldrin, α-chlordane, γ-chlordane, dacthal, *p,p′*-DDE, *p,p′*-DDT, heptachlor, lindane, methoxychlor) and 5 PCB congeners commonly found in environmental samples (PCBs 105, 138, 153, 170, and 180). Acid-extractable analytes included pentachlorophenol and 4 other compounds. All extracts were analyzed using gas chromatography/mass spectrometry (GC/MS) in selected ion monitoring (SIM) mode; analyte amounts were quantified using the internal standard method.

The usual detection limits were as follows: 20.8 ng/g of dust for dacthal, α-chlordane, γ-chlordane, heptachlor, DDE, DDT, and PCBs; 83.3 ng/g for aldrin; 83.5 ng/g for pentachlorophenol; and 104 ng/g for dieldrin. Changes in analytic procedures during the study resulted in increased detection limits for lindane (from 41.4–128 ng/g) and methoxychlor (from 20.7–62.5 ng/g). Dust samples weighing less than 2 g had detection limits that were higher than the usual detection limits.

Laboratory spikes of 27 dust samples showed that all organochlorine analytes were efficiently extracted, with recovery means ranging from 89% to 106% and recovery standard deviations from 9% to 19%, except for pentachlorophenol (74% ± 20%), DDT (130% ± 26%), and methoxychlor (140% ± 27%). Reported levels in dust were not adjusted for spike recoveries. Analysis of laboratory splits of 27 dust samples (unblinded) showed close agreement between the regular sample and the split. The measurements for 89% of the 122 detection pairs agreed within 20%, and 98% agreed within 40%. Confirmation analyses performed by full-scan GC/MS on 55 samples generally verified the large SIM results, indicating that the analytes had been properly identified.

Data Imputation and Statistical Analysis

Preliminary analyses indicated that the measured analyte concentrations were consistent with lognormal distributions. The laboratory measurements contained various types of missing (or "interval-measured") data where precise concentrations were not determined, primarily when the concentration was below the minimum level detected by the GC/MS technique. We also encountered interval-measured data when the sample contained compounds that coeluted with the target analyte ("interferences"). We applied a multiple-imputation procedure[21] to create a complete dataset for all analytes that were present in at least 10% of the samples (α-chlordane, γ-chlordane, DDE, DDT, pentachlorophenol, and the 5 PCB congeners); we excluded methoxychlor because of a disproportionately high number of samples with interferences. Analytes detected in fewer than 10% of the samples were not considered further. We first set an upper and lower bound for each interval-measured datum. We assumed (and found no evidence to the contrary) that there was nothing intrinsically unique about the interval-measured values; that is, we assumed that they derived from the same distributions that generated the measured values. Using all detected and interval-measured values in controls, we developed a prediction equation using Tobit regression for the logarithm of each analyte concentration on study site, age, sex, education, presence of an Oriental rug, and year the home was built (using PROC LIFEREG in the SAS System for Windows, version 8.2; SAS Institute Inc., Cary, NC). The multiple imputation approach created 5 plausible datasets by randomly inserting values for interval-measured values based on the regression equations. The procedure was adapted from the "fill-in" approach described by Helsel,[22] applied by Moschandreas et al,[23] and discussed further by Colt et al[20] and Lubin et al.[24] In the current study, the imputation parameters were based on controls only to reflect characteristics of the general population.[25]

Statistical analyses were based on measured and imputed values for α-chlordane, γ-chlordane, DDT, DDE, pentachlorophenol, and the 5 PCB congeners. All computations were performed using SAS for Windows, version 8.2. Spearman correlation coefficients between congeners were estimated. We used multivariate linear regression models to estimate the effects of demographic variables, study center, presence of an Oriental rug, and age of the home on organochlorine levels in dust. Because the analyte concentrations were consistent with a lognormal distribution, the dependent variable in the linear regression models was the natural logarithm of the analyte level.

We estimated the relative risk of developing NHL by deriving adjusted odds ratios (ORs) and 95% confidence intervals (CIs) from multiple logistic regression models. For analyses of several histologic types, we used polytomous regression. Regression models included study center, sex, education (<12 years, 12–15 years, ≥16 years), and age (<45 years, 45–64 years, ≥65 years). We first estimated NHL risk for each analyte based on whether the measured or imputed values were above or below the usual detection limit, and then grouped individuals with values above the detection limit into tertiles based on concentrations in the controls. Tests of trend were performed using the mean concentration of the analyte among the controls in each tertile. We conducted similar analyses with total PCBs using individuals whose dust had undetectable levels of all PCBs as the referent.

We fitted each linear and logistic regression model 5 times using the 5 different datasets developed using the multiple imputation approach, and then combined the results according to the method described by Little and Rubin[21] using the MIANALYZE procedure in SAS. Because this approach correctly accounts for the variance from the imputation, it results in wider confidence intervals than would be obtained from a single-imputation approach.

Most of imputations were performed to derive concentrations for levels below the usual detection limit (Table A1, available with the electronic version of this article). In the risk analysis, these were all included in the referent category; therefore, the imputed concentrations had no effect on the odds ratios. Only those values imputed for the other types of interval-measured data were meaningful in the estimation of risk. Approximately 3% of the values in the final dataset were imputed for nondetects with raised detection limits due to limited dust quantities (84.5–316 ng/g for pentachlorophenol; 21.2–56.3 ng/g for other compounds), and interferences oc-

curred infrequently except for DDT and PCB 105 (16% and 7%, respectively). Note that all imputed values, even those below the usual detection limit, were included in the multiple linear regression models estimating the effects of demographic and other variables on organochlorine levels in dust.

RESULTS

Subjects with analyzed dust samples were like the NHL study population as a whole, disproportionately elderly and typically living in single-family homes (Table 1). Because people must have owned their carpets for at least 5 years to be eligible for dust sampling, people with dust samples generally had lived in their current home longer and were slightly older, compared with the overall study population.

α-Chlordane and γ-chlordane, the major constituents of technical chlordane formulations, were highly correlated in the controls' dust samples (Spearman correlation coefficient = 0.998), as were DDT and its degradation product

TABLE 1. Characteristics of Study Participants

	NHL Study Participants With Dust Samples			All NHL Study Participants*
	Cases (n = 603)	Controls (n = 443)	Total (n = 1046)	Total (n = 1966)
Study center; %				
Detroit	18	13	16	21
Iowa	32	33	32	32
Los Angeles	21	20	21	20
Seattle	29	34	31	28
Age (years); %				
<45	11	9	10	15
45–64	47	37	43	45
65+	42	54	47	40
Sex; %				
Male	54	52	53	52
Female	46	48	47	48
Education (years); %				
<12 yr	8	9	8	9
12–15 yr	66	60	64	60
≥16 yr	26	31	28	31
Years in current home; median	21	20	20	16
Type of home; %				
Single family	85	81	84	81
Duplex/townhouse	6	7	6	6
Apartment	6	7	7	10
Other/unknown	2	5	3	3
Year home built†				
<1940	22	23	22	
1940–1959	29	23	26	
1960–1979	33	34	33	
1980+	16	20	18	
Unknown	<1	<1	<1	
Any Oriental rugs†				
Yes	15	18	16	
No	85	82	84	

*All white subjects interviewed.
†Asked only of participants who provided dust samples.

DDE (0.72). All of the PCB congeners were correlated with one another (0.51–0.99).

In the multivariate linear regression models, age of the home was a strong determinant of organochlorine levels, with the highest concentrations found in homes built before 1960 and the lowest in homes built after 1980 (Table 2). Homes with Oriental rugs had, on average, 70% more chlordane, 90% more DDT, and 40% more DDE than homes without Oriental rugs. Geographic differences included relatively high levels of chlordane in Los Angeles, PCBs in Seattle and Detroit, and pentachlorophenol in Iowa and Seattle. Education positively correlated with DDT and PCBs.

There was a 30% elevation in NHL risk if DDE was detected in the dust (CI = 1.0–1.7) (Table 3). A 50% excess risk was observed if any of the PCB congeners was detected (1.2–2.0). Individual congeners with the highest ORs were PCB 153 (1.4; 1.1–1.8), PCB 170 (1.5; 1.0–2.1), and PCB 180 (1.5; 1.1–2.0). When levels above the usual detection limit were divided into tertiles (referent = levels below the usual detection limit), NHL risk was elevated in the top tertiles of both DDE (1.6; 1.1–2.2) and PCB 180 (1.7; 1.1–2.6), and in the top 2 tertiles of total PCBs (for middle tertile, 1.6 [1.1–2.4]; for top tertile, 1.5 [1.0–2.2]). There were significant positive trends in risk with increasing concentrations of DDE and PCB 180 (P trend = 0.02 and 0.03, respectively). There was no evidence of an association with DDT. Risks at the highest tertile of exposure were modestly elevated for chlordane and some of the other compounds. Although contaminant levels in dust were strongly influenced by the age of the home, this was not a confounder. None of the parameter estimates in Table 3 differed by more than 15% when age of the home was included in the model. We examined the joint effects of these 2 variables on NHL risk and found no significant interactions.

Detection of PCB 180 was associated with elevated NHL risk in all 4 study areas (Detroit, 1.3 [0.6–2.9]; Iowa, 1.3 [0.8–2.1]; Los Angeles, 2.6 [1.1–6.1]; Seattle, 1.5 [0.9–2.4]) and in both sexes (men, 1.5 [1.0–2.3]; women, 1.5 [0.9–2.3]) (data not shown). PCB 180 risk was elevated after adjustment for the other PCB congeners, many of which were

TABLE 2. Association of Explanatory Variables With Organochlorine Concentrations (Natural Log) in Dust for Controls Only; Parameter Estimates (Exponentiated) From Multiple Linear Regression Models

	α-Chlordane	DDE	DDT	Pentachlorophenol	PCB 180	PCB Sum
Study Center						
Detroit*	1.0	1.0	1.0	1.0	1.0	1.0
Iowa	1.5 (0.8–2.8)	1.0 (0.7–1.6)	1.5 (0.9–2.5)	1.7 (1.2–2.5)	0.9 (0.4–1.7)	0.5 (0.3–1.0)
Los Angeles	4.4 (2.1–9.0)	1.0 (0.6–1.5)	0.9 (0.5–1.7)	0.7 (0.4–1.0)	0.6 (0.2–1.7)	0.3 (0.1–0.7)
Seattle	1.1 (0.6–2.0)	0.7 (0.5–1.1)	0.9 (0.5–1.5)	1.8 (1.3–2.7)	1.4 (0.6–2.9)	1.0 (0.5–1.9)
Sex						
Men*	1.0	1.0	1.0	1.0	1.0	1.0
Women	1.2 (0.7–1.9)	0.9 (0.7–1.2)	1.3 (1.0–1.8)	1.0 (0.8–1.3)	0.9 (0.6–1.2)	1.0 (0.7–1.4)
Education (years)						
<12*	1.0	1.0	1.0	1.0	1.0	1.0
12–15	1.0 (0.5–2.3)	1.1 (0.7–1.8)	1.1 (0.6–2.1)	1.0 (0.6–1.5)	1.3 (0.6–2.9)	1.3 (0.7–2.7)
>15	1.1 (0.5–2.5)	1.2 (0.7–1.9)	1.6 (0.8–3.1)	1.1 (0.7–1.7)	1.5 (0.6–3.4)	1.8 (0.8–4.0)
Age at diagnosis or selection (years)						
<45*	1.0	1.0	1.0	1.0	1.0	1.0
45–64	1.3 (0.6–2.8)	0.9 (0.5–1.4)	1.0 (0.5–1.8)	1.1 (0.7–1.8)	1.0 (0.5–2.2)	1.0 (0.5–2.1)
65+	1.7 (0.8–3.6)	1.0 (0.7–1.6)	1.6 (0.9–2.9)	1.9 (1.2–2.9)	1.5 (0.7–3.3)	1.5 (0.7–3.2)
Oriental rug						
No*	1.0	1.0	1.0	1.0	1.0	1.0
Yes	1.7 (1.0–3.0)	1.4 (1.0–2.0)	1.9 (1.2–2.9)	1.3 (0.9–1.8)	1.3 (0.7–2.3)	1.1 (0.6–2.1)
Year home built						
1980 or later*	1.0	1.0	1.0	1.0	1.0	1.0
1960–1979	1.5 (0.8–2.6)	1.6 (1.1–2.3)	2.3 (1.5–3.6)	2.2 (1.6–3.0)	2.0 (1.1–3.7)	2.7 (1.6–4.7)
1940–1959	4.1 (2.1–7.9)	3.1 (2.2–4.6)	5.1 (3.1–8.4)	2.7 (1.9–3.8)	2.2 (1.0–4.9)	3.5 (1.8–6.9)
<1940	1.6 (0.8–3.2)	3.2 (2.1–4.9)	8.7 (5.3–14)	2.2 (1.5–3.1)	2.4 (1.3–4.5)	3.6 (2.0–6.4)

*Reference category.

TABLE 3. Risk of NHL in Relation to Detection of Organochlorines and Tertiles of Detected Concentrations in Dust Samples

Organochlorine Concentration (ng/g)	No. of Cases*	No. of Controls*	Odds Ratio†	(95% CI)	P for Trend
α-Chlordane					
Below UDL	368	283	1.0	—	—
Above UDL	235	160	1.2	(0.9–1.5)	
20.8–40.8	61	52	0.9	(0.6–1.3)	
41.1–117	90	54	1.4	(0.9–2.0)	
120–5870	84	54	1.3	(0.8–1.9)	0.30
γ-Chlordane					
Below UDL	315	244	1.0	—	—
Above UDL	288	199	1.2	(0.9–1.5)	0.18
20.8–43.2	88	67	1.0	(0.7–1.5)	
43.3–118	95	66	1.2	(0.8–1.7)	
119–8710	105	66	1.3	(0.9–1.9)	
DDE					
Below UDL	304	249	1.0	—	—
Above UDL	299	194	1.3	(1.0–1.7)	0.02
20.8–34.9	94	64	1.3	(0.8–1.8)	
35.0–55.9	83	65	1.1	(0.7–1.6)	
56.7–2450	122	65	1.6	(1.1–2.2)	
DDT					
Below UDL	197	130	1.0	—	—
Above UDL	406	313	0.9	(0.7–1.2)	0.09
20.8–98.7	124	104	0.8	(0.6–1.2)	
99.0–248	111	105	0.8	(0.5–1.1)	
251–24,600	170	104	1.2	(0.8–1.6)	
Pentachlorophenol					
Below UDL	71	54	1.0	—	—
Above UDL	528	387	1.2	(0.8–1.8)	0.14
83.5–292	197	129	1.3	(0.8–2.0)	
295–668	145	129	1.0	(0.7–1.6)	
672–57,500	186	129	1.4	(0.9–2.2)	
PCB 105					
Below UDL	486	368	1.0	—	—
Above UDL	117	75	1.2	(0.9–1.7)	0.74
20.8–31.0	40	24	1.3	(0.8–2.2)	
31.3–73.0	43	26	1.4	(0.8–2.4)	
75.8–3860	34	25	1.1	(0.6–1.9)	
PCB 138					
Below UDL	398	305	1.0	—	—
Above UDL	205	138	1.3	(1.0–1.7)	0.95
20.8–33.6	64	46	1.2	(0.8–1.8)	
33.7–84.2	83	46	1.6	(1.1–2.4)	
84.9–10,200	58	46	1.1	(0.7–1.7)	

(Continued)

TABLE 3. Risk of NHL in Relation to Detection of Organochlorines and Tertiles of Detected Concentrations in Dust Samples *(Continued)*

Organochlorine Concentration (ng/g)	No. of Cases*	No. of Controls*	Odds Ratio†	(95% CI)	P for Trend
PCB 153					
Below UDL	351	280	1.0	—	—
Above UDL	252	163	1.4	(1.1–1.8)	0.34
20.8–32.9	74	54	1.2	(0.8–1.7)	
33.1–74.2	101	55	1.7	(1.2–2.5)	
74.5–6460	77	54	1.3	(0.9–2.0)	
PCB 170					
Below UDL	509	389	1.0	—	—
Above UDL	94	54	1.5	(1.0–2.1)	0.17
20.8–28.3	30	18	1.4	(0.8–2.6)	
28.6–52.9	31	18	1.5	(0.8–2.7)	
53.7–1380	33	18	1.5	(0.8–2.7)	
PCB 180					
Below UDL	432	338	1.0	—	—
Above UDL	171	105	1.5	(1.1–2.0)	0.03
20.8–31.6	52	35	1.3	(0.8–2.1)	
31.8–54.5	55	35	1.5	(0.9–2.3)	
55.3–2870	64	35	1.7	(1.1–2.6)	
All PCBs					
All Below UDL	315	262	1.0	—	—
Any Above UDL	288	181	1.5	(1.2–2.0)	0.14
21.9–82.5	88	57	1.4	(0.9–2.1)	
82.5–202.8	114	63	1.6	(1.1–2.4)	
203.8–23,380	92	61	1.5	(1.0–2.2)	

*The distribution of cases and controls among the concentration categories varies slightly among the 5 imputed data sets. The distribution presented here is an example from one set of imputed values.
†Adjusted for study center, sex, age, and education.
UDL, usual detection limit.

highly correlated (1.3; 0.8–2.0). DDE detection was associated with excess risk in 3 of the study areas (Detroit, 0.8 [0.4–1.6]; Iowa, 1.3 [0.9–2.1]; Los Angeles, 1.7 [1.0–2.9]; Seattle, 1.5 [0.9–2.5]), and the association was stronger among men (1.6; 1.1–2.3) than women (1.1; 0.7–1.5).

We examined NHL risk by histologic subtype (Table 4). In general, organochlorines in dust conferred a greater risk of developing T-cell lymphoma than the other histologic subtypes, although the number of patients with T-cell lymphoma was small (n = 36). Individuals with at least one PCB

TABLE 4. Risk of NHL and Detection of Organochlorines in Dust by Histologic Subtype of NHL

Histology	No. of Cases*	α-Chlordane OR (95% CI)	DDE OR (95% CI)	DDT OR (95% CI)	PCB 180 OR (95% CI)	Any PCB OR (95% CI)
Follicular	156	1.1 (0.7–1.7)	1.3 (0.9–2.0)	1.0 (0.7–1.6)	1.5 (1.0–2.4)	1.7 (1.2–2.5)
Diffuse	189	1.2 (0.8–1.7)	1.3 (0.9–1.9)	0.8 (0.5–1.1)	1.1 (0.7–1.7)	1.3 (0.9–1.9)
T-cell	36	1.8 (0.8–3.7)	2.6 (1.3–5.4)	2.8 (1.1–7.1)	1.6 (0.7–3.6)	2.0 (1.0–4.0)
Other	206	1.1 (0.8–1.6)	1.2 (0.8–1.6)	0.8 (0.5–1.1)	1.8 (1.3–2.7)	1.6 (1.1–2.2)
All cases	587	1.2 (0.9–1.5)	1.3 (1.0–1.7)	0.9 (0.7–1.2)	1.5 (1.1–2.0)	1.5 (1.2–2.0)

*Subtype-specific results exclude 16 cases from Los Angeles with unknown histology.

congener were at increased risk for follicular and "other" lymphomas.

DISCUSSION

We found evidence of associations, including dose–response trends, between NHL risk and concentrations of PCB 180 and DDE in carpet dust. People whose carpet dust contained detectable levels of any of the 5 PCB congeners had higher NHL risk than people whose dust contained no PCBs, but there was no consistent dose–response pattern; findings were similar for PCB 153 and PCB 170.

We know of no other studies of NHL risk and organochlorine levels in carpet dust. Previous studies with biologic samples have generally found increased risk among individuals with higher concentrations of PCBs in blood or adipose tissue. Hardell et al[10] found higher levels of total PCBs (36 congeners) in blood from NHL cases than controls in Sweden. For PCBs considered by Moysich et al[26] to be immunotoxic (sum of 11 congeners), levels above the median conveyed a 3-fold increase in NHL risk.[10] In a nested case–control study in Maryland, Rothman et al[11] observed a strong dose–response relationship between total PCBs (28 congeners) in serum and NHL risk. Congener-specific analyses of these data showed dose–response trends for PCB 105 and PCB 138; for PCB 180, there was an 80% increase in risk in the highest quartile (unpublished data). In a small hospital-based case–control study, Hardell et al[12] examined individual PCB congeners in adipose tissue, including the 5 addressed in the current study. Levels of all 5 congeners were higher in cases than controls, but the differences were not statistically significant. In a nested case–control study of adipose tissue samples collected from cadavers and surgical patients between 1969 and 1983, no association between PCB levels and NHL risk was found,[27] although there were important methodologic limitations to the study. Occupational studies of capacitor-manufacturing workers[28–31] and a study of Swedish fisherman who consume PCB-contaminated fish[32] show only weak and inconsistent evidence of increased risk of lymphohematopoietic malignancies; none of these studies collected biologic samples.

PCBs may increase the risk of NHL through their dioxin-like effects, immunotoxicity, ability to induce mixed-function oxidases,[33–35] or their demonstrated ability to act as tumor promoters.[36] The ability of PCBs to cause immunologic changes in humans is intriguing, because immunosuppression is a recognized risk factor for NHL.[11,37] The biologic activities of PCBs differ by congener, and the mechanisms of toxicity of specific congeners are unclear. Three congeners measured in this study (PCBs 105, 138, and 170) are proposed to be immunotoxic.[35] PCB 180 (as well as PCBs 153 and 170) is proposed to be a cytochrome P450 enzyme inducer and may produce toxicity through bioactivation.[33]

Although diet the major source of human exposure to PCBs today, their presence in carpet dust provides evidence of exposure through other sources that may have been high in the past. Before PCBs were banned, they could have been released from everyday products such as fluorescent lighting fixtures, television sets, and refrigerators,[15] from pesticides applied in or near the home,[16] and from building sealants,[15] potentially resulting in exposure through inhalation or dermal contact. Several studies indicate that indoor concentrations of PCBs are higher than outdoor levels.[15,38]

Our results for DDE were less consistent. An association was observed only in men, the dose–response relationship was not monotonic, and the concurrent finding of no association for DDT is difficult to explain. This discrepancy could be related to data quality issues (DDT lab spike recovery 130% ± 26%), with a relatively high prevalence of samples with interferences, or to DDT's lower vapor pressure, making it less likely than DDE to volatilize and adsorb to indoor surfaces and contribute to exposure. Another possibility is that treatment of carpets with DDT by manufacturers makes dust measurements of this compound less effective as an exposure indicator. We were unable to determine the prevalence of this practice. This would not have strongly affected DDE levels in the dust, because environmental degradation of DDT to DDE is accelerated in the presence of sunlight, moisture, and microorganisms, factors which are normally absent in the carpet dust environment.

Epidemiologic studies of DDT exposure have generally found modest elevations in NHL risk. Hardell et al[10] found a 20% increase in NHL risk among individuals with DDE levels in adipose tissue/blood above the median. Similarly, Rothman et al[11] found that NHL increased weakly with increasing serum concentrations of DDT equivalents (predominantly *p,p′*-DDE), and the association substantially weakened when adjusted for PCB exposure. Quintana et al[27] reported increasing NHL risk with increasing DDE levels in adipose tissue samples, but the association was attenuated when other pesticides were included in the model. Two case–control studies[5,39] without biologic samples also observed associations between NHL risk and DDT use, which diminished when adjusted for exposure to other substances. Cantor et al[7] reported an excess of NHL among farmers reporting DDT use. Several other case–control interview studies reported increases in NHL risk among people exposed to DDT.[4,6,8,9] No association was found in a population-based case–control study in Sweden.[40] DDT has been shown to be carcinogenic in laboratory animals, and suggested mechanisms include direct mutagenicity through the formation of DNA adducts, promotion of preexisting abnormal cells, or cytotoxicity leading to hyperplasia and promotional tumor development.[18]

There is no ready explanation for the stronger relationship between organochlorine exposure and risk of T-cell

lymphomas compared with other histologic subtypes. Although detection of organochlorines conferred a greater risk of developing T-cell lymphoma than the other histologies, risk was elevated for the other histologies as well.

The chief strengths of this population-based case–control study are the large number of participants with dust samples and the use of an objective measure of exposure. A weakness is the loss of information from death, inability to locate, refusal, or absence of eligible carpets. Bias could occur if, on balance, these factors were strongly related to both organochlorine levels in dust and disease status. Death was the major reason for nonparticipation among cases, and if organochlorine exposure shortens survival, we may have underestimated risk. Refusal and unlocatability were the main reasons for nonparticipation among controls. If nonparticipating controls had higher organochlorine levels than those who participated, we may have overestimated risk. However, participation rates often increase with level of education, and in our study, education was positively correlated with PCB levels in dust.

Another limitation is the uncertainty in using carpet dust samples to measure historic exposure to organochlorine compounds. Carpet dust is probably not an important route of exposure for adults. Carpet dust samples are used mainly as a historic record of chemicals used in the home or entering the home. Dust sampling does not indicate the source of the chemical or when it entered the carpet, and it is therefore a crude indicator of exposure. Finally, carpet dust sampling has little bearing on dietary ingestion, a major source of exposure to these compounds. On the other hand, this tool has important advantages over questionnaire- and biologically-based approaches. Carpet dust samples are objective measures of exposure, unaffected by difficulties or biases in recall of past activities. Carpet dust samples are unaffected by factors that may influence body burdens of chemicals such as age, body mass index, reproductive history, breast feeding, serum cholesterol, individual variation in PCB elimination, and (of primary importance in a case–control study) disease status or treatment.

In conclusion, our findings suggest an increased risk of NHL associated with exposure to PCBs, with evidence of greater effects for PCB 180. Our data also provide some evidence that DDE can contribute to this risk. Additional research is needed to evaluate how well carpet dust samples represent historic exposure to organochlorine compounds.

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